

Mandible matrix necrosis in beagle dogs After 3-years of daily oral bisphosphonate treatment

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[Allen, Matthew R.](#) ; [Burr, David B.](#)



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Abstract:

Purpose An increasing number of reports have implicated bisphosphonates as contributing to osteonecrosis of the jaw. The goal of this study was to evaluate mandible necrosis in beagle dogs treated for 3 years with oral alendronate (ALN). **Materials and Methods** Skeletally mature female beagles were treated daily for 3 years with oral doses of vehicle (VEH) or ALN (0.20 or 1.0 mg/kg/day). These doses approximate, on a mg/kg basis, those used for postmenopausal osteoporosis and Paget's disease, respectively. At necropsy, the second molar region of the mandible was excised, stained en bloc with basic fuchsin, and assessed for matrix necrosis and intracortical bone turnover rate using histology. Matrix necrosis was defined as a region greater than 500 μm^2 that was void of basic fuchsin stain, assessed using both bright-field and confocal microscopy. **Results** No animals developed exposed bone lesions in the oral cavity during the 3-year study. Matrix necrosis was observed in 25% of ALN0.2 animals, 33% of ALN1.0 animals, and was noticeably absent from all vehicle animals (P < .05 pooled ALN doses vs VEH). These necrotic regions occurred predominately in the alveolar bone and were clearly void of patent canaliculi. Intracortical bone turnover rate of the alveolar mandible bone region was

significantly lower (–75%, P < .05) in ALN-treated animals compared with VEH. Conclusions Three years of daily oral bisphosphonate treatment reduces bone turnover significantly and increases the incidence of matrix necrosis within the mandible of dogs.

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